Abstract of the Disclosure

A method and apparatus for measuring binding between a plurality of molecules of a biological receptor protein and a plurality of molecules of a type which binds to said biological receptor is presented. Apparatus utilizes a sensor possessing a waveguide to which have been attached in close proximity to its surface, features resembling molecules having binding affinity for said biological receptor. Light is injected into said waveguide so as to produce an evanescent field at its surface. Molecules of receptor protein are tagged with a tag belonging to that class of chemicals which alters a characteristic of light, when said light passes through said chemical tag. Apparatus utilizes a rapid means of monitoring the change in optical signal coming from the waveguide as binding proceeds between tagged receptor protein and the binding molecular feature of the waveguide. This allows direct measurement of binding and dissociation rates between the receptor and the binding feature of the waveguide. By using a waveguide having a feature resembling a ligand for the receptor, the potential hormonal activity of a test substance may be evaluated from its ability to compete with the waveguide for binding with the receptor. The effect of a test compound on binding of receptor protein to a subsequent element in a hormonal signal transduction mechanism is evaluated by measuring the impact of the test compound on binding between receptor protein and a feature resembling said next element of the signal transduction mechanism. Methods are provided whereby such data may be used to compute affinity constants, binding activity, complex affinity constants resulting from cooperativity, and kinetic parameters for the receptor and test ligand and for the receptor and the next element of the signal transduction mechanism. Preferred embodiments of the invention illustrate application of the method and apparatus to measuring binding between biological receptors and their nuclear response elements, and the use of this type of measurement for assessment of the activity of estrogen mimics present in a test sample, and for evaluation of pharmaceuticals intended to treat hormone dependent cancers.